marked up version of the changes made to the claims by the instant Amendment captioned "Version with Markings to Show Changes Made".

Claim Rejections - 35 U.S.C. § 102

Claim 21 stands rejected for allegedly being anticipated by Adams et al. under 35 U.S.C. § 102. The Examiner states that Adams "teaches applicants compound in propylene glycol...a liquid". Applicant respectfully traverses this rejection as it applies to the claims as amended.

Claim 21 has been cancelled. Claim 15 has been amended to incorporate the composition forms included in claim 21 except for "a liquid". Therefore this rejection is moot as applied to the claims as amended. Applicant respectfully requests that the rejection under 35 U.S.C. § 102 be withdrawn and that the claims be allowed.

Claim Rejections - 35 U.S.C. § 103

Claims 15-18 stand rejected for allegedly being obvious over Adams in view of Peat under 35 U.S.C. § 103. Applicant respectfully traverses this rejection.

The Examiner alleges that the claimed compound was "considered for a pharmaceutical purpose" based on Adams et al. The Examiner states that Peat "merely teaches that these types of compounds can be administered in a form of a tablet or pill...or capsules".

Three criteria must be met to establish a case of *prima facie* obviousness: (1) there must be some suggestion or motivation to modify or combine references, (2) there must be a reasonable expectation of success, and (3) the references must teach or suggest all the claim limitations. The teaching or suggestion to make the combination and the reasonable expectation of success must both be found in the cited art, not the applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d

1438 (Fed. Cir. 1991). These criteria are not met for the claimed invention.

The claimed invention is drawn, *inter alia*, to an effective pharmaceutical composition for treating tumors. A reasonable reading of the cited references (Adams et al. and Peat) indicates that taken together they satisfy none of the three criteria stated above.

First, the references do not teach or suggest all the claim limitations. Neither Adams et al. nor Peat teach or suggest the claim limitation of an effective pharmaceutical composition for treating tumors. A fair reading of Adams et al. shows that the claimed compound was never considered for a pharmaceutical purpose. The focus of the paper is on establishing the etiology of human breast cancer (See, the abstract & Introduction, pg 4036), not on discovering pharmaceuticals.

Although the claimed steroid was tested as part of a group of C19 steroids as "possible inhibitors of estrogen sulfotransferase" (See, the abstract, page 4036), nowhere do the authors indicate that inhibition of estrogen sulfotransferase is expected to identify a potential pharmaceutical. Instead, the authors are interested in the etiology of disease, including the role of sulfotransferases.

The only section in the Discussion relating to estrogen sulfotransferase is provided below (page 4039, end of first column to top of second column):

> "A mentioned earlier, steroid sulfotransferase activities in human breast tumors correlate with prognosis. A situation in which the ratio of DHEAS to estradiol sulfate is <1, reflecting a poor prognosis (12), may be due to the low levels of DHEA sulfotransferae observed in many tumors (3). Such a situation would lead to higher intracellular levels of free DHEA which, in turn, would be expected to inhibit the sulfurylation of estrogen (Chart 4) and thus maintain its concentration.
>
> A scheme summarizing the possible involvement of DHEA-DHEAS at the level of the

tumor cell is shown in Chart 5." (Emphasis added.)"

Nothing in this section relates to the identification or testing of a pharmaceutical. It is simply a proposed etiology of the disease incorporating their new data.

Nothing in Peat satisfies the deficiencies in Adams et al. As the Examiner states, Peat "merely teaches that these types of compounds can be administered in a form of a tablet or pill...or capsules". Peat does not suggest 5-androstene-3β,17α-diol as a pharmaceutical. Therefore, the Examiner has failed to make a prima facie case for obviousness, and this rejection cannot stand.

Second, there is no suggestion or motivation to modify or combine references. Adams et al. teaches one assay in which 5-androstene-3β,17α-diol, as well as other steroids including DHEA, was tested. In this assay of estrogen sulfatase inhibition, DHEA exhibited high inhibition (page 4038, column 2), whereas 5-androstene-3β,17α-diol showed basically no inhibition (See, Table 1). The authors never discuss the activity of 5-androstene-3β,17α-diol or its potential as a pharmaceutical. The authors provide absolutely no suggestion or motivation to test 5-androstene-3β,17α-diol for pharmaceutical activity. Thus, the authors provide no motivation to modify or combine references.

Third, the references do not indicate that there is a reasonable expectation of success. In the only assay in which 5-androstene-3β,17α-diol was tested, the estrogen sulfatase assay, 5-androstene-3β,17α-diol showed no activity. This certainly indicates no reasonable expectation of success in the development of a pharmaceutical using this compound.

In summary, the requirement for making a prima facie case of obviousness has not been met. Therefore, Applicant respectfully requests that the rejection of claims 15-18 under 35

U.S.C. § 103 for allegedly being obvious, be withdrawn, and that the claims be allowed.

Claim Rejections - 35 U.S.C. § 112, second paragraph

Claims 21 and 24 stand rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite. The Examiner states that "claim 21 and claim 24 fail to find basis in claims 15 and 19 drawn to the form of a tablet or capsule." Applicant respectfully traverses this rejection as it applies to the claims as amended.

Claim 21 has been cancelled rendering this rejection moot as to claim 21.

Claim 24 is dependent on claim 19. Claim 19 is not limited by the phrase "the form of a capsule or tablet." The compound is said to be "part of a cyclodextrin inclusion complex." Claim 22 adds the limitation to claim 19 of "the form of a tablet." Claim 23 adds the limitation to claim 19 of "the form of a capsule." Therefore, claim 24 which specifies other forms of the composition of claim 19, does have basis and further limits the scope of claim 19.

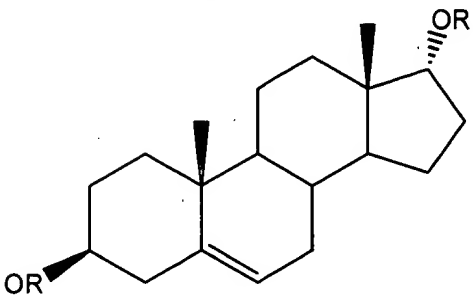
Based on the above, Applicant respectfully requests that the rejection under 35 U.S.C. § 112, second paragraph, be withdrawn and that the claims be allowed.

Claim Rejections - 35 U.S.C. § 112, first paragraph

Claims 15-24 stand rejected under 35 U.S.C. § 112, first paragraph for allegedly not being enabled. The Examiner states that "the specification, while being enabling for the specific tumors disclosed, does not reasonably provide enablement for the term "tumors"...one skilled in the art could not use the entire scope of the claimed invention without undue experimentation." Applicant respectfully traverses this rejection.

First, the Examiner's attention is drawn to allowed claim 11 of U.S. Patent No. 5,912,240, of which this application is a continuation, provided below:

11. A sterile composition of matter comprising a tumor proliferation inhibiting effective amount of αAED or an ester or ether thereof of the formula:



wherein R may be H, alkenyl of 2-8 carbons, alkyl of 1-8 carbons, phenylalkyl of 1-4 carbons, phenyl and COR_2, wherein R_2 is H, alkyl of 1-8 carbons, alkenyl of 2-8 carbons, phenylalkyl wherein the alkyl has 1-4 carbons (including benzyl) or phenyl, and any phenyl moiety may have up to three substitutents chosen from among hydroxy, carboxy of 1-4 carbons, halo, alkoxy of 1-4 carbons, alkyl of 1-4 carbons or alkenyl of 2-4 carbons and wherein any alkyl may be a straight chain, branched chain, or the alkyl may be wholly or partially cyclized, in a sterile solution appropriate for parenteral administration.

Based on the allowance of the above claim in the parent application for this case, Applicant asserts that the term "tumors" is enabled and that the rejection should be withdrawn.

Second, factors to be considered to determine whether any necessary experimentation is undue include: 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Based on an analysis of these factors, Applicant asserts that the claims are enabled.

Although the Examiner asserts that the breadth of the claims is "extreme" and that the "cancer therapy art remains highly unpredictable", in fact claims that encompass a compound or a class of compounds for the treatment of cancer are common. See, for example, claim 11 of U.S. Patent No. 5,912,240, of which this application is a continuation, provided above. Therefore, Applicant asserts that the first five factors should not be construed against the claims at issue.

The Examiner also alleges that there is a "lack of guidance and working examples" and that "undue experimentation" would be required to use the entire scope of the claimed invention. In fact, examples are provided in the specification showing the activity of the compound against three different tumors: breast (See, for example, paragraph 24), lymphoid (See, for example, paragraph 40) and myeloma (See, for example, paragraph 41). A list of tumors is provided in paragraph 22 of the specification. Other examples provide guidance for the preparation of formulations (See, for example, paragraphs 38, 39, 42-47, and 52-56). Finally, undue experimentation is not required based on Example 1 of U.S. Patent Application No. 09/794,531 (Publication No. US-2001-0046980-A1) that shows the activity of this compound in prostate cancer in rats.

Based on the above, Applicant respectfully requests that the rejection under 35 U.S.C. § 112, first paragraph be withdrawn and that the claims be allowed.

SUMMARY

In view of the above, Applicant asserts that the claimed invention is in condition for allowance and notification to that effect is respectfully requested. In order to facilitate rapid allowance, the Examiner is invited to contact the undersigned at the telephone number below.

Any fees due in relation to the filing of this Response are hereby authorized to be deducted from Deposit Account No. 501536.

Respectfully submitted,

Date: Nov. 22, 2002

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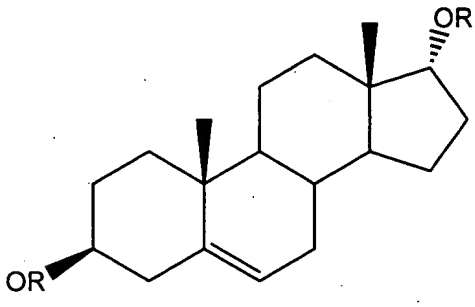
VERSION WITH MARKINGS TO SHOW CHANGES MADE

15. (Four Times Amended) A composition of matter for inhibiting tumors comprising a tumor inhibiting effective amount of 5-androstene-3β,17α-diol or an ester or ether thereof of the formula:



wherein R is selected from [a] the group consisting of H, alkenyl of 2-8 carbons, alkyl of 1-8 carbons, phenylalkyl of 1-4 carbons, phenyl and COR_2, wherein R_2 is selected from [a] the group consisting of H, alkyl of 1-8 carbons, alkenyl of 2-8 carbons, phenylalkyl wherein the alkyl has 1-4 carbons (including benzyl) and phenyl, and wherein any phenyl moiety may have up to three substitutents selected from the group consisting of hydroxy, carboxy of 1-4 carbons, halo, alkoxy of 1-4 carbons, alkyl of 1-4 carbons[,] and alkenyl of 2-4 carbons, and wherein any alkyl [may be a] is selected from the group consisting of straight chain, branched chain[, or the alkyl may be] and wholly or partially cyclized, and wherein said [formulation] composition is [being] in [the] a form selected from the group consisting of a capsule [or], a tablet, a lozenge, a spray, a cream, a jelly, a suppository, a douching solution and an adhesive patch.

24. (Once Amended) The composition of claim 19, wherein said composition is in a form selected from the group consisting of a lozenge, a spray, a cream, a jelly, a suppository, a douching solution, a liquid and an adhesive patch.